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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,207	10/27/2003	Ekambar R. Kandimalla	HYB-005US7	3842

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WAYNE A. KEOWN
SUITE 1200
500 WEST CUMMINGS PARK
WOBURN, MA 01801

EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/694,207	KANDIMALLA ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,28,29,34,35,71 and 72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26, 28-29, 34-35 and 71-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 21 April 2009 has been entered.

2. Claims 1-25, 27, 30-33 and 36-70 are cancelled.

Claims 26 and 34 have been amended.

Claims 71-72 have been added.

3. Claims 26, 28-29, 34-35 and 71-72 are under consideration.

4. This Office Action contains New Grounds of Rejections.

Rejections Maintained and New Grounds of Rejections

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The rejection of claims 26, 28-29, 34-35 and now applied to newly added claims 71-72 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The response filed 4/21/09 states that CpG-containing oligonucleotides lost immunostimulatory activity if the CpG was eliminated or if the cytosine was replaced by 5'-methylcytosine and thus, the CpG dinucleotide is the sole structure requirement to generate the immune response. Applicants' state that their contribution was the surprising discovery that replacement of cytosine in a CpG dinucleotide of an immunostimulatory CpG-containing

oligonucleotide by cytosine analogue (C*) as presently recited does not abolish the immune stimulatory activity. Applicant states that the office action goes to great lengths to describe all the possible modifications that could be made to a CpG-containing oligonucleotide to alter the immunomodulatory properties of the CpG-containing oligonucleotide, however, applicant asserts that this is not relevant to the claims since the claims do not require changes outside the CpG. Applicant states that changes outside the CpG can be made, however, these changes are not enough as an active CpG motif is required. Applicants' arguments have been fully considered but are not found persuasive. Applicants' argument that the an unmethylated CpG dinucleotide is the sole structure requirement to generate the immune response is not found persuasive because the art also recognizes that methylated CpG oligonucleotides as well as non-CpG oligonucleotides rich in thymidine have immunostimulatory effects (Vollmer et al, Antisense and Nucleic Acid Drug Development, 12:165-175, 2002, cited on PTO-892 mailed 3/31/08). Vollmer et al also indicate that the immunostimulatory properties were also highly dependent upon phosphorothioate (PS) backbone chemistry, in addition to base content and length of the PS oligonucleotides. Again, the instant application does not provide a correlation between the common structure C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil and a common function, i.e., generate an immune response in a patient or treat caner in a patient.

Applicant also argues that the instant specification sets forth six immunostimulatory oligonucleotides (e.g., see pp. 5-6 of the reply), each distinguished by the C* modification. While each of the six olignucleotides pointed to by applicant have a different C* modification and in a sense can be considered a different oligonucleotide, then issue remains that each one comprises a single oligonucleotide sequence (i.e., 5'-CTATCTGACGTTCTCTGT-3'). The instant application does not describe any other immunostimulatory oligonucleotides comprising the formula CpG into which the C* modification is incorporated that function to stimulate an immune response and also treat cancer in a patient. In fact, the instant application does not administer the immunostimulatory oligonucleotide (i.e., 5'-CTATCTGACGTTCTCTGT-3') comprising the formula C*pG, wherein C* is 5-hydroxycytosine, 5-hydroxymethylcytosine or N4-ethylcytosine for the treatment of cancer in a patient. Applicants' position appears to be that no description of the genus of immunostimulatory oligonucleotides comprising the formula

C*pG, wherein C* is 5-hydroxycytosine, 5-hydroxymethylcytosine or N4-ethylcytosine that effectively treat any and all cancer is required. The structures of the immunostimulatory oligonucleotides comprising the formula C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil that generate an immune response in a patient or treat caner in a patient are not known and the genus is inclusive to a variety of subgenera having disparate structures and functions. Thus, the instant disclosure does not provide sufficient written description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus or various subgenera of immunostimulatory oligonucleotides comprising the formula C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil that generate an immune response in a patient or treat caner in a patient. See *Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1406. The instant application does not provide a correlation between the common structure C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil and a common function, i.e., generate an immune response in a patient or treat caner in a patient. Again, the specification discloses that a CpG oligonucleotide comprising the cytosine analogs, particularly 5-hydroxycytosine or N4-ethylcytosine, can be modulated significantly by incorporating appropriate chemical modifications in the 5'-flanking sequence, suggesting that these cytosine analogs in a CpG-motif are recognized as part of an immunostimulatory motif. As discussed supra, the relevant CpG immunostimulatory oligonucleotide art teaches that the length, sequence, backbone modification and methylation status can alter the immunostimulatory properties of CpG oligonucleotides. Vollmer et al (Antisense and Nucleic Acid Drug Development, 12:165-175, 2002, cited on PTO-892 mailed 3/31/08) teach that both thymidine content and length of thymidine stretches affect CpG-mediated immunostimulation and oligonucleotides with methylated CpG motifs have length-dependent immunostimulatory effects (e.g., see pg. 173 and Figs. 2-4). Vollmer et al also discloses that poly-G sequences have independent immune effects and can modulate the activity of CpG motifs in either an agonistic or antagonistic fashion (see

pg. 166 2nd col.). Verthelyi et al (The Journal of Immunology, 168:1659-1663, 2002, cited on PTO-892 mailed 8/6/07) states that "[D]ue to evolutionary divergence in CpG recognition between species, ODN that are highly active in rodents are poorly immunostimulatory in primates, and vice versa" (e.g., pg. 1659, left col.) and "CpG ODN that activate human immune cells in vitro are only weakly immunostimulatory in mice" (e.g., pg. 1662, Discussion, first par.). Dittmer et al (Current Opinion in Microbiology, 6:472-477, 2003, cited on PTO-892 mailed 8/6/07) reports that "[U]nfortunately, CpG-ODN that optimally stimulate mouse cells were only weakly effective in human cells, thus they could not be used for the treatment of humans" (e.g., pg. 472, right col., bottom par.). Thus, one of skill in the art could not predict the operability of any other species of immunostimulatory oligonucleotides comprising an immunostimulatory dinucleotide having the formula C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil other than those disclosed. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]. " See *Enzo Biochem*, 323 F.3d at 966, 63 USPQ2d at 1615; *Noelle v. Lederman*, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when … the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed."

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical

structure of the encompassed genus of genus of immunostimulatory oligonucleotides comprising the formula C*pG, or the various subgenera of immunostimulatory oligonucleotides comprising the formula C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil that generate an immune response in a patient or treat caner in a patient, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Applicant is reminded that the written description requirement is separate and distinct from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

For these reasons and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 71-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 71 and 72 recites the limitation "the oligonucleotide analog immunostimulatory compound". There is insufficient antecedent basis for this limitation in the claim. Base claims 26 and 34, respectively, do not recite an oligonucleotide analog immunostimulatory compound.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 34-35 and 72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of stimulating an immune response in a patient comprising administering to the patient an immunostimulatory oligonucleotide comprising the formula C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil and G is guanosine, does not reasonably provide enablement for a method of treating a cancer in a patient comprising administering to the patient an immunostimulatory oligonucleotide comprising the formula C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil and G is guanosine and wherein the method further comprises administering a vaccine or a DNA vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CAFC 1988).

Wands states on page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to methods of stimulating an immune response in a patient and treating a cancer in a patient comprising administering to the patient an immunostimulatory oligonucleotide comprising the formula C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil and G is guanosine and wherein the

method further comprises administering a vaccine or a DNA vaccine. Thus, the scope of the claims broadly encompass treating any and all cancers in patients comprising administering any immunostimulatory oligonucleotide comprising the formula C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil and G is guanosine, encompassing thousands or millions of oligonucleotides that differ in length and sequence. The specification teaches that the immunostimulatory oligonucleotide 5'-CTATCTGACGTTCTCTGT-3' in the absence of C* elicits an immune response that is equal to or greater than the immune response elicited when C* is present and selected from 5-hydroxycytosine, 5-hydroxymethylcytosine and 4-thiouracil. The specification does not teach the treatment of any cancer in a subject comprising administering immunostimulatory oligonucleotide comprising the formula C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil and G is guanosine and wherein the method further comprises administering a vaccine or a DNA vaccine. There are no working examples of the treatment of any cancer in a subject comprising administering an immunostimulatory oligonucleotide comprising the formula C*pG, wherein C* is selected from 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine and 4-thiouracil and G is guanosine and wherein the method further comprises administering a vaccine or a DNA vaccine. Thus, the scope of the claims is extremely broad compared to the guidance and exemplification provided in the specification. *In re Fisher* , 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (" [T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.".

The state of the art with regard to cancer therapy is unpredictable, in addition CpG immunostimulatory nucleic acid molecules in cancer therapy is unpredictable. Donnelly et al (Nature Medicine, 2003, Vol. 9, pages 1354-1356) teaches that over many decades various approaches to eliciting both innate and acquired immune responses against tumors have been tried, some with a degree of success. However, immunotherapy has yet to be incorporated into first-line therapies for more than a very few types of cancers such as the use of IL-2 immunotherapy for metastatic renal cell carcinoma (p. 1354, col. 2). Further, Donnelly teaches that treating cancer with something that looks more like a modern-day vaccine, with a defined antigen and an optimized adjuvant and delivery platform, is still in the future (see p. 1354, col. 2;

see also col. 3). "A variety of anti-tumor vaccine clinical trials have been undertaken. In spite of the large number of these trials, and the plethora of distinct approaches investigated, there has been little evidence of clinical efficacy. Furthermore, precise correlates of clinical effects and immunological responses have been lacking." (DeGruijl et al, Nature Medicine, 1999, Vol. 5, pages 1124-1125, see p. 1124, col. 1). Bitton (Current Opinion in Molecular Therapeutics, 2004, Vol. 6, pages 17-26) teaches that developing cancer vaccines to treat solid tumors is not an easy task (abstract). Bitton teaches that "immune editing", in part, explains why many cancer vaccines work in animal models but not in a clinical setting (abstract). Bitton describes the various cancer vaccine strategies and evaluates the evidence supporting their efficacy (abstract). Bitton indicates that the final picture with regard to cancer vaccines is confusing and comparison of different vaccine strategies is almost impossible because of the different strategies from different groups.

Further, most of the vaccines are still experimental and their clinical utility is almost negligible (abstract). Bitton teaches that therapeutic vaccines have proved to have little use in cancer treatment and that in fact in almost every well-designed, well-controlled, randomized phase III trial, they have failed to demonstrate any significant improvement in overall or disease-free survival (p. 17, col. 2; Table 2). "It is clear that most vaccines are indeed effective immunogens, but they do not seem to be effective at triggering anticancer responses. Tumor size reduction, the classic endpoint in clinical development of cytotoxic drugs does not seem to be useful in evaluating cancer vaccines; tumor stabilization might be more valuable. Finally, there is no evidence of improvement in overall survival or disease-flee survival. The implementation of well-designed randomized phase III trials is urgently required." (pp. 24-25) This is just an example of the state of the art for cancer treatments.

With regard to CpG in the treatment of cancers, Weiner (Leukocyte Biology, 2000. Vol. 68, pages 455-463) indicates that there is therapeutic potential in cancer treatment for CpG as an immune adjuvant (Table 1) and that there are a number of scenarios where CpG could be used as a component of cancer immunotherapy, each of these areas is under intensive investigation (p. 458, col. 1). Studies in a tumor model (38C13 murine lymphoma) indicate that CpG was just as effective as CFA at inducing an antigen-specific antibody response (p. 458, col. 2). Weiner teaches that "[P]reliminary studies suggest CpG ODN can be effective in a variety of scenarios

when used alone or in combination with other agents. Despite this promise we still do not understand the molecular mechanisms responsible for the immunostimulatory effects of CpG ODN. All CpG ODN are not alike, and more needs to be learned about the heterogeneous responses that occur based on host organism, cell subset, or CpG ODN sequence. Most importantly, we have not yet explored their clinical effects. Further work with CpG ODN in both the laboratory and the clinic is needed before we can know their true promise as investigational immunological and therapeutic agents." (p. 461, col. 1). Krieg et al (Nature, 1995. Vol. 374, pages 546-549) teaches that CpG has NK-stimulating properties and suggest that it can be used in immunotherapy of tumors, yet Krieg et al also indicates that many or even most types of tumors are relatively resistant to NK-mediated lysis (p. 117, col. 2). Ballas et al (Journal of Immunology, 2001. Vol. 167, pages 4878-4886) teaches that the selection of optimal CpG ODN for cancer immunotherapy depends upon a careful analysis of the cellular specificities of various CpG motifs and an understanding of the cellular mechanisms responsible for the antitumor activity in a particular tumor (abstract). Ballas et al teaches that a single CpG ODN cannot be used to treat all cancers and tumors. Although several CpG ODN were active as sole immunotherapeutic agents in two tumor models, different motifs were optimal in each model. CpG ODN 1585 was optimal against B16 melanoma and its effects were dependent on NK cells. CpG ODN 1826 was optimal in a lymphoma model and its effects appeared to require NK (early) and T cells (late). These results illustrate that the therapeutic potential of distinct CpG motifs should be custom-tailored for each desired immune effect (p. 4878, col. 2; see also p. 4885, col. 1). Agrawal et al (TRENDS in Molecular Medicine, 2002. Vol. 8, pages 114-120) also teaches that different effects are observed with different CpG ODNs. Verthelyi et al (The Journal of Immunology, 168:1659-1663, 2002, cited on PTO-892 mailed 8/6/07) states that "[D]ue to evolutionary divergence in CpG recognition between species, ODN that are highly active in rodents are poorly immunostimulatory in primates, and vice versa" (e.g., pg. 1659, left col.) and "CpG ODN that activate human immune cells in vitro are only weakly immunostimulatory in mice" (e.g., pg. 1662, Discussion, first par.). Dittmer et al (Current Opinion in Microbiology, 6:472-477, 2003, cited on PTO-892 mailed 8/6/07) reports that "[U]nfortunately, CpG-ODN that optimally stimulate mouse cells were only weakly effective in

human cells, thus they could not be used for the treatment of humans" (e.g., pg. 472, right col., bottom par.).

> Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson* , 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. *Genentech Inc. v. Novo Nordisk A/S,* 42 USPQ2d 1001, 1005 (CAFC 1997).

In view of the lack of the predictability of the art to which the invention pertains as evidenced by Donnelly et al, DeGruijl et al, Britton, Weiner, Krieg et al, Ballas, Agrawal et al, Verthelyi et al, and Dittmer et al the lack of guidance and direction provided by applicant, and the absence of working examples, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the immunostimulatory CpG oligonucleotides effectively treat any cancer.

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643